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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 02122004

Application Number: 09/918,359
Filing Date: July 30, 2001
Appellant(s): WALKE ET AL.

David W. Hibler
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 2, 2003.

*(1) **Real Party in Interest***

A statement identifying the real party in interest is contained in the brief.

*(2) **Related Appeals and Interferences***

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

*(3) **Status of Claims***

The statement of the status of the claims contained in the brief is correct.

*(4) **Status of Amendments After Final***

No amendment after final has been filed.

*(5) **Summary of Invention***

The summary of invention contained in the brief is essentially correct, except the asserted utilities for the claimed invention are in dispute.

*(6) **Issues***

The appellant's statement of the issues in the brief is correct.

*(7) **Grouping of Claims***

Appellant's brief includes a statement that the claims stand or fall together.

*(8) **Claims Appealed***

The copy of the appealed claims contained in the Appendix to the brief is correct.

*(9) **Prior Art of Record***

Doerks et al. Protein annotation: detective work for function prediction. Trends in Genetics. June 1998, Vol. 14, No. 6, pages 248-250.

Bork et al. Go Hunting in sequence databases but watch out for the traps. Trends in Genetics 1996, 12:425-427

Brenner et al. Errors in Genome Annotation. Trends in Genetics 1999, 15:132-133

Voet et al. Biochemistry. 1990. John Wiley & Sons, Inc. pages 126-128 and 228-234

Adams et al. EST180740 Jurkat T-cells V Homo sapiens cDNA 5' end, mRNA sequence. Accession No. AA309878. 19-APR-1997.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-9 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed patentable utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance. Appellant is directed to MPEP § 2107.

It is clear from the instant specification that the nucleic acid encoding the NHP polypeptide has been isolated because of its similarity to known proteins. However, it is commonly known in the art that sequence-to-function methods of assigning protein function are

prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). Furthermore, Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

After complete characterization, this protein may be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Appellant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson,* 148 USPQ 689 (Sup. Ct., 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation.

However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 USC § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an Applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a nucleic acid encoding a polypeptide which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as NHP, the instant invention is incomplete. In the absence of knowledge of the natural substrate or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which inhibit its activity is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for NHP then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

Claims 1, 5-9 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

A. Do claims 1 and 5-9 lack a patentable utility?

According to MPEP § 2107, a rejection for lack of utility is imposed when an invention lacks an asserted specific and substantial utility for the claimed invention and it does not have a readily apparent well-established utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.

In the Brief at page 5, Appellant argues that the present nucleic acid sequences have utility in diagnostic assays such as in forensic analysis. The Brief also lists several polymorphisms disclosed by Appellant in the Specification. Appellant further argues that forensic analysis does not require any information at all about the ultimate biological activity of the encoded protein (Brief at 6). Appellant further argues that the disclosed polymorphisms are useful to distinguish 50% of the population, because it is an inherent property of any polymorphic marker to be able to distinguish 50% of the population (Brief at 6). Appellant argues that the nucleic acid of the instant claims can be used in diagnostic assays for polymorphisms, which is a real world utility. This asserted utility is credible but not specific or substantial. The specification discloses a number of polymorphisms present in the NHP gene (see Specification at 15-16). However, the specification does not disclose the nexus between any of these polymorphisms and any function of the expressed polypeptide. Additionally, there is no correlation disclosed between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or condition, therefore this

asserted utility is not specific. Significant further experimentation would be required of the skilled artisan to identify individuals with a disease or disorder which correlates to the presence of one of the enumerated polymorphisms, therefore, since this asserted utility is not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Appellant further argues that the use of these polymorphisms in forensic analysis is a real world utility. However, the asserted utility of using the polynucleotides in forensic analysis is not specific. Such assays can be performed with any polynucleotide. The use of the claimed nucleic acid in forensic analysis is not particular to the sequence being claimed because it would be applicable to the general class of nucleic acids, because no correlation has been shown to the polymorphisms disclosed in the NHP gene, and any state or condition. The fact that polymorphisms exist in this gene and could be used for forensic analysis is not a specific utility for this gene, since polymorphisms exist in many genes, and could be use for forensic analysis. The specificity of the utility would arise upon the showing of a correlation of the polymorphism with a diseased state or condition for which it would be useful to identify a population.

Appellant further argues that the Examiner has confused the requirement for a specific utility with an alleged need for a "unique" utility, and Appellant cites Carl Zeiss Stiftung v. Renishaw PLC, 945 F.2d 1173, 20 USPQ2d 1094 (Fed. Cir. 1991) which sets forth that "an invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications". However, Carl Zeiss is inapposite to the facts of the instant case. In Carl Zeiss, the district court had found that a claim to a probe containing a stylus which is mounted to a movable arm above a table which supports an object to be measured

lacked utility because "the arbitrary presentation of part of an invention does not constitute a claim of a valid invention" and that the claimed device could not function as a probe. See Carl Zeiss at 1180. In the instant case, however, the claims lack utility not because they are incomplete, and not because they do not set forth the best or only way to accomplish a result, and not because they are not unique, but because they do not have either a well-established utility or a specific and substantial asserted utility.

Appellant asserts that forensic analysis is used to distinguish individual members of the human population from one another based simply on the presence or absence of one of the described polymorphisms (Brief at 9). However, the use of the claimed polynucleotides in a method of forensic analysis is not a specific utility because there is no correlation between the presence of any of the polymorphisms and any state or condition, and there is no correlation disclosed between the presence of any of these polymorphisms and the effect of the presence of any of these polymorphisms on the risk of any disease or disorder, therefore this asserted utility is not specific or substantial. Additionally, the Specification does not set forth the frequency with which these polymorphisms occur in the general population, thus the utility of the nucleic acid for forensic analysis is not complete since additional experimentation would be required. Such a utility is considered a research utility only designed to identify a particular function of the claimed sequences and is not a substantial utility. See, e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility." Appellant cites In re Brana, and argues that as in Brana, "Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is

well before it is ready to be administered to humans." However, the nucleic acids of the instant claims are not being claimed as pharmaceuticals, and the nucleic acid is not a lead compound which must be further refined through further experimentation. Appellant is arguing that the nucleic acid is useful in a method of forensic analysis, while the Specification does not set forth the frequency with which these polymorphisms occur in the general population, and what populations they would be able to distinguish. In the instant case considerable further research would be required to determine a specific and substantial utility for the claimed polynucleotide by correlating the polymorphisms to a disease state or other condition which it would be useful to classify a population. Furthermore, the claims are drawn to polynucleotides which encode the amino acid of SEQ ID NO: 7, and the alleged utility of the nucleic acid in an method of forensic analysis would not provide a utility for nucleic acids encoding a protein or the protein encoded thereby.

Appellant further argues (Brief at 12) that a sequence sharing nearly 100% percent identity at the protein level over extended portions of the claimed sequence is presented the leading scientific repository for biological sequence data (GenBank), and had been annotated by third party scientists wholly unaffiliated with Appellants as "Homo sapiens two-pore calcium channel protein 2", GenBank accession number AY029200. Appellant argues that this demonstrates that those skilled in the art would thus conclude that the claimed nucleic acid sequence encodes an ion channel protein. However, the annotated protein has not been shown to function as a calcium channel, and the art recognizes the assignment of function based on homology is inherently difficult, as evidenced by the references of Doerks, Brenner and Bork.

According to MPEP 2107, in order for Applicant to rebut the rejection for lack of utility imposed because the invention lacks an asserted specific and substantial utility for the claimed invention and it does not have a readily apparent well-established utility, Applicant must provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established at the time of filing. In the instant case, even if the AY029200 polynucleotide is found to function as a Calcium channel, the date of publication of the sequence is May 1, 2002, which is after the filing date of the instant application. In order for an asserted utility to be well-established, it must be well-established at the time of filing. Since the AY029200 polynucleotide is a post-filing reference, the asserted utility was not well-established at the time of filing.

Further according to MPEP 2107, the examiner should also ensure that there is an adequate nexus between the evidence and the properties of the now claimed subject matter as disclosed in the application as filed. That is, the applicant has the burden to establish a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention. In the instant case, at the time of filing the instant nucleic acids were not disclosed as encoding specifically calcium channels, but only described as encoding generically as ion channels (see Specification at 1, lines 9-12). There are many types of ion channels, including potassium, sodium, calcium and chloride channels, and there are a wide variety of each of these types of channels. The fact that the Specification only describes the encoded polypeptide as an ion channel demonstrates that at the time of filing, Appellant did not know the type of channel, if any, the encoded polypeptide would make. Since the originally disclosed properties of the claimed invention are only set forth as encoding an ion channel, there is not a probative

relationship between the submitted evidence of the encoded polypeptide allegedly functioning as a calcium channel, and the disclosed properties of the encoded polypeptide being an ion channel.

The Doerks, Brenner and Bork references were cited by the Examiner to demonstrate that based upon the art recognized errors inherent in sequence-function methods of assigning protein function, and the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex, and the fact that the change of a single amino acid can radically alter protein function, and absent sufficient evidence to the contrary, a preponderance of the evidence demonstrates that the nucleic acid encoding a polypeptide with an amino acid sequence as set forth in SEQ ID NO: 7 lacks a well-established, specific and substantial utility. Appellant argues that the use of these references is not persuasive. Appellant argues that the Doerks reference teaches that utilization of family information and thus a more detailed characterization "' should lead to simplification of update procedures for the entire families if functional information becomes available for at least one member" Doerks, page 248, paragraph bridging columns 1 and 2, emphasis added). Appellants argue that the AY029200 sequence is nearly 100% identical to the encoded SEQ ID NO: 7 and thus demonstrates the utility of the claimed polynucleotide. However, as noted above, the annotation of the AY029200 sequence as a calcium channel was published post-filing, and thus the utility was not well-established at the time of filing, and furthermore, there is not a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention, since the encoded polypeptide was only described as an ion channel, not a calcium channel. In addition, it is not clear that the AY029200 polypeptide was ever demonstrated to be a calcium channel, which is exactly the situation the Doerks reference was

cited to show. The Doerks reference teaches that inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). Thus, while Appellant is relying on the AY029200 polypeptide to show the utility of the claimed encoding polynucleotide, it is not clear that the function of the AY029200 polypeptide is actually known, since the Doerks reference is relevant as it teaches that sequence-to-function methods of assigning protein function are prone to errors.

Appellant argues that the Brenner reference does not support the rejection for lack of utility since it teaches that the main problems in using homology to predict function are solvable by use of modern and accurate sequence comparison procedures. However, for a comparison to be effective the function of the protein to which it is compared must be known. Here the function of the AY029200 polypeptide is open to question, and furthermore, even if it is a calcium channel, it was not disclosed as a calcium channel in the Specification as filed.

Appellant argues that the Bork reference is inapposite since the AY029200 polypeptide is nearly 100% identical to the encoded SEQ ID NO: 7. However, as above, the function of the AY029200 polypeptide as a calcium channel is not shown, and furthermore, there is no disclosure that the encoded SEQ ID NO: 7 is a calcium channel.

Appellant argues that the instant case is analogous to Example 10 of the "Revised Interim Utility Guidelines Training Materials Examples" (Guidelines), in that the very fact that the sequence of Example 10 has sequence similarity with a known protein possessing well-established utility is sufficient to confer a specific, substantial, and credible utility upon the claimed sequence. However, Example 10 is inapposite to the facts of the instant case. Unlike the DNA ligases shown in Example 10, which have a well-established use in ligating DNA, here

the nucleic acids encode a polypeptide for which there is not a well-established use. Appellant attempts to establish a use for the encoded polypeptide by claiming it is highly homologous to a protein reported in the art to be a calcium channel, but that function is not demonstrated, and additionally, that function was not well-established at the time of filing of the instant application.

Appellant further argues that the claimed nucleic acid sequence have utility in assessing gene expression in a DNA array or gene chip, and cites several issued U.S. patents covering the gene chip technology. However, use of the claimed polypeptide in an array for selectivity screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility that would apply to virtually ever member of a general class of materials, such as any collection of DNA. Even if the expression of Appellant's individual polynucleotide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polynucleotide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what use any expression information regarding this polynucleotide could be put. Despite Appellant's arguments, this is not a confusion of a specific utility with the alleged need for a "unique" utility. Any nucleotide sequence can be put on a DNA array and then this array can be screened to determine whether the expression pattern correlates with a disease state or condition. This is not a specific utility for this nucleic acid. A specific utility for this nucleic acid would be a correlation between expression of the specific

nucleic acid in a disease state or some other condition which would be useful to know. That has not been demonstrated here.

Beginning at the third paragraph of page 17 of the Brief, Appellant argues that the claimed polynucleotide sequences have utility in "determining the genomic structure", "identification of protein coding sequence", and "identification of exon splice junctions" and provide biologically validated empirical data that specifically define that portion of the corresponding genomic locus that actually encodes exon sequence. Appellant newly cites the Venter reference to allegedly demonstrate the significance of expressed sequence information in the structural analysis of genomic data.

This has been fully considered but is not deemed to be persuasive because such a utility is considered a research utility only designed to identify a particular function of the claimed sequences and is not a substantial utility. See, e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966) wherein a research utility was not considered a "substantial utility." While the Examiner agrees with the Appellant on the scientific value of the claimed polynucleotide sequences and on the significance of expressed sequence information in structural analysis of genomic data, such a use of the polynucleotide sequences in gene mapping does not represent a specific and substantial utility. The exhibit and the publication cited by the Appellant merely show that the significance of expressed sequences in the structural analysis of genomic data; they do not show that the present polynucleotide sequences have a patentable utility.

Beginning at page 19 of the Brief, Appellant summarizes case law on the utility requirement. Citing case law, Appellant urges that the present claims clearly meet the

requirement of 35 U.S.C. §101. The essential disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility.

Appellant's arguments have been fully considered but are not deemed to be persuasive for the following reasons. First, the statement, "(t)o violate §101 the claimed device must be totally incapable of achieving a useful result." Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), indicates that a rejection under 35 U.S.C. § 101 for lack of operability can be overcome by a showing of actual use or commercial success. The claimed invention in the instant case is drawn to nucleic acid sequences, not a device; the instant rejection under 35U.S.C. §101 is not directed to inoperativeness of a device, rather to a lack of patentable utility of the claimed nucleic acid sequences; and the instant issue is whether the asserted utilities meet the three-pronged test for a patentable utility.

Secondly, since the specification fails to disclose a specific, substantial utility or a well-established utility, the present claims do not satisfy the utility requirement of 35 U.S.C. §101. Merely citing case laws on the utility requirement does not render a patentable utility for the present invention. While "anything under the sun that is made by man" is patentable, it does not necessarily mean the present invention is patentable. In fact, the present invention is not patentable due to lack of a patentable utility.

Furthermore, while the FDA approval is not a prerequisite for finding a compound useful within the meaning of the patent laws, and the requirement for the utility of the claimed invention is different from the FDA standard for drug approval, 35 U.S.C. §101 does require a specific, substantial, and credible utility, or well-established utility for an invention. Such a utility has to be a "real world " context of use which does not require significant further research.

Appellant confuses this requirement with the "further research and development" needed in pharmaceutical composition and drug development. In other words, a patentable utility has to be clearly identified or immediately apparent in the specification, whereas some "further research and development" is permitted in drug development. For example, determining optimal dosages or drug tolerance in human is further research and development, which is acceptable under 35 USC 101 because it is not significant. On the other hand, determining a specific disease to be treated by a drug constitutes significant further research and development, which is not acceptable under 35 U.S.C. §101.

In the instant case, the specification fails to disclose the biological functions, physiological significance, or any specific and substantial utility of the claimed molecules. Without such information, how can one in the skilled art use the claimed invention in a meaningful manner? See Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Finally, at page 20 of the Brief, Appellant challenges the legality of the Patent Examination Utility Guidelines and the validity of issued US patents. It is noted that an Examiner has no authority to comment on the legality of the Guidelines and the validity of US Patents.

Appellant concludes this section by urging that the rejection of claims 1, and 5-9 under 35 U.S.C. § 101 must be overruled. The Examiner believes that the rejections should be sustained for the reasons set forth above.

B. Are claims 1 and 5-9 unusable due to a lack of patentable utility?

As Appellant indicates at page 16 of the Brief, a rejection under U.S.C. § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under 35 U.S.C. § 101.

Therefore, for reasons set forth above, Appellant's arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility. For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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February 18, 2004

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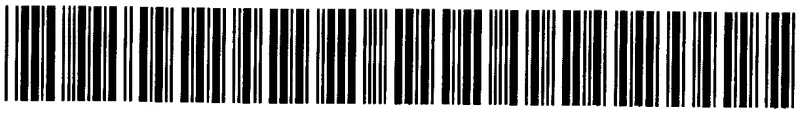

Creation date: 03-04-2004
Indexing Officer: SMOHAMMED - SUAD MOHAMMED
Team: 1600PrintWorkingFolder
Dossier: 10130539

Legal Date: 03-04-2004

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